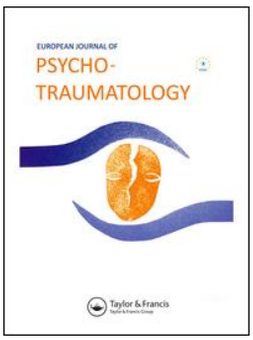

European Journal of Psychotraumatology

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/zept20

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To cite this article: Kali S. Barawi , Catrin Lewis , Natalie Simon & Jonathan I. Bisson (2020) A systematic review of factors associated with outcome of psychological treatments for post-traumatic stress disorder, European Journal of Psychotraumatology, 11:1, 1774240, DOI: 10.1080/20008198.2020.1774240

To link to this article: https://doi.org/10.1080/20008198.2020.1774240

Published online: 01 Jul 2020.

EUROPEAN JOURNAL OF PSYCHOTRAUMATOLOGY
2020, VOL. 11, 1774240
https://doi.org/10.1080/20008198.2020.1774240

EUROPEAN JOURNAL OF PSYCHO-TRAUMATOLOGY
THE OFFICIAL JOURNAL OF THE EUROPEAN SOCIETY FOR TRAUMATIC STRESS STUDIES

Taylor & Francis
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REVIEW ARTICLE

A systematic review of factors associated with outcome of psychological treatments for post-traumatic stress disorder

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ABSTRACT

Objective: Psychological interventions for post-traumatic stress disorder (PTSD) are not always effective and can leave some individuals with enduring symptoms. Little is known about factors that are associated with better or worse treatment outcome. Our objective was to address this gap.

Method: We undertook a systematic review following Cochrane Collaboration Guidelines. We included 126 randomized controlled trials (RCTs) of psychological interventions for PTSD and examined factors that were associated with treatment outcome, in terms of severity of PTSD symptoms post-treatment, and recovery or remission.

Results: Associations were neither consistent nor strong. Two factors were associated with smaller reductions in severity of PTSD symptoms post-treatment: comorbid diagnosis of depression, and higher PTSD symptom severity at baseline assessment. Higher education, adherence to homework and experience of a more recent trauma were associated with better treatment outcome.

Conclusion: Identifying and understanding why certain factors are associated with treatment outcome is vital to determine which individuals are most likely to benefit from particular treatments and to develop more effective treatments in the future. There is an urgent need for consistent and standardized reporting of factors associated with treatment outcome in all clinical trials.

Una revision sistematica de los factores asociados con los resultados de los tratamientos psicologicos para el trastorno de estres postraumático

Objetivo: Las intervenciones psicológicas para el trastorno de estrés postraumático (TEPT) no son siempre efectivas y pueden dejar a algunos individuos con síntomas permanentes. Se sabe poco acerca de los factores que se han asociado con mejores o peores resultados del tratamiento. Nuestro objetivo fue abordar este vacío.

Método: Llevamos a cabo una revisión sistemática siguiendo las Pautas de Colaboración de Cochrane. Incluimos 126 ensayos controlados aleatorizados (RCTs por sus siglas en ingles) de intervenciones psicológicas para TEPT y examinamos los factores que estuvieron asociados con el resultado del tratamiento, en términos de severidad de síntomas de TEPT postratamiento, y recuperación o remisión.

Resultados: Las asociaciones no fueron ni consistentes ni fuertes. Dos factores se asociaron con reducciones más pequeñas en la severidad de síntomas de TEPT postratamiento: el diagnóstico comórbido de depresión y mayor severidad de los síntomas de TEPT en la evaluación inicial. Los niveles de educación más alta, la adherencia a las tareas y la experiencia de un trauma más reciente se asociaron con mejores resultados del tratamiento.

Conclusión: La identificación y comprensión de por qué ciertos factores se asociaron con los resultados del tratamiento es vital para determinar qué individuos se podrían beneficiar de determinados tratamientos y desarrollar en el futuro, tratamientos más efectivos. Existe una necesidad imperiosa de un reporte consistente y estandarizado de los factores asociados con los resultados de los tratamientos en todos los estudios clínicos.

对创伤后应激障碍心理治疗结果相关因素的系统综述

目的：创伤后应激障碍（PTSD）的心理干预并不总是有效的，有时会给一些个体留下持久的症状。对于与治疗结果更好或更差的相关因素知之甚少。我们旨在解决此差距。

方法：我们根据Cochrane协作指南进行了系统综述。我们纳入了126项PTSD心理干预的随机对照试验（RCT），并就治疗后PTSD症状严重程度及恢复或缓解情况，考查了与治疗结果相关的因素。

结果：关联既不一致也不强健。两种因素与治疗后PTSD症状严重程度降低程度较小有关：与抑郁的共病诊断和基线评估的高PTSD症状严重程度。高教育水平、坚持家庭作业和最近的创伤经历与更好的治疗结果相关。

ARTICLE HISTORY
Received 1 March 2020
Revised 28 April 2020
Accepted 8 May 2020

KEYWORDS
Psychological intervention; randomized control trial; post-traumatic stress disorder; treatment outcome

PALABRAS CLAVE
Intervención psicológica; Ensayo controlado aleatorizado; Trastorno de Estrés Postraumático; Resultado de tratamiento

关键词：
心理干预; 随机对照试验; 创伤后应激障碍; 治疗结果

HIGHLIGHTS

- This systematic review is the first to demonstrate factors associated with outcome of psychological treatment for PTSD.
- This review provides potential treatment targets as well as informing future research assessing factors associated with psychological therapies for PTSD.

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结论：识别和理解为什么某些因素与治疗结果相关，对于确定哪些人最有可能从特定治疗中受益以及未来开发更有效的治疗至关重要。亟需与全部临床试验治疗结果相关的一致且标准化因素的报告。

1. Introduction

Post-traumatic stress disorder (PTSD) is a debilitating psychiatric disorder with an estimated lifetime prevalence of 7.8% (Kessler et al., 2005). PTSD results from experiencing or witnessing traumatic events that involve actual or threatened death, serious injury, or sexual violence (American Psychiatric Association, 2000). A proportion of trauma-exposed individuals recover without treatment, while a third of those who initially develop PTSD and receive treatment remain symptomatic for 3 years or longer Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995). Despite significant improvements in PTSD treatment, the complex psychopathology and frequency of co-morbid conditions such as depression can make PTSD difficult to treat (Coffey, Stasiewicz, Hughes, & Brimo, 2006) and suboptimal outcome or even treatment failure are not uncommon (Watts et al., 2013b). Understanding why people do better or worse in treatment is imperative and can inform us on the most effective treatments for individuals (Durham et al., 2005; Foa, 2011).

A number of psychological therapies have been evaluated in the treatment of PTSD. Trauma-focused therapies such as exposure-based interventions (Foa, 2011), cognitive-based treatment (Ehlers & Clark, 2008), and Eye Movement Desensitization and Reprocessing (Shapiro, 2014) have been investigated most extensively and shown to be the most effective (Bisson, Roberts, Andrew, Cooper, & Lewis, 2013). Whilst psychological therapies perform reasonably well for many patients, recent estimates suggest that up to 50% of people with PTSD who engage in treatment fail to respond adequately (Resick et al., 2017). Furthermore, 10%–20% of individuals from the general population and 20–40% of military veterans exposed to trauma, experience PTSD symptoms that persist and are associated with impairment despite treatment (Hall et al., 2019) (Rauch et al., 2018). It is not clear why treatments work more or less well for different people with PTSD and there is an urgent need to accurately identify factors that moderate treatment outcome in PTSD.

Enhancing understanding of factors associated with treatment outcome is important for several reasons. First, this knowledge can be helpful in determining treatment choice, especially because not all patients respond to first-line psychological interventions (Watts et al., 2013a). Second, increased knowledge may lead to insight into the fundamental processes underlying treatment and facilitate adaptations or the development of new approaches that improve outcomes. Third, clinicians will be enabled to adjust current treatment delivery and planning, in order to reduce poor response.

The aims of this review were to: (a) undertake the first comprehensive systematic review of factors associated with poor treatment outcome in randomized controlled trials (RCTs) of psychological treatments for individuals with PTSD, and (b) use a narrative synthesis to develop a description of common factors associated with outcome.

2. Methods

The protocol for this systematic review was published via PROSPERO (Barawi, Lewis, Hoskins, Simon, & Bisson, 2017).

This was a systematic review of RCTs. The standards for the conduct of Cochrane Intervention Reviews (MECIR) (Chandler, Churchill, Higgins, Lasserson, & Tovey, 2012) were implemented. A narrative synthesis was conducted in accordance with the 'Guidance on the Conduct of Narrative Synthesis in Systematic Reviews' (Popay, Sowden, Petticrew, Arai, & Rodgers et al., 2006).

2.1. Selection criteria

The review included RCTs of any defined psychological therapy aimed at the reduction of PTSD-symptoms in comparison with a control group (e.g. treatment as usual/waiting list), other psychological therapy, or psychosocial intervention (e.g. psychoeducation/relaxation training). To be included in the narrative synthesis, data needed to be available regarding factors associated with treatment outcome. There was no restriction on the type of analysis used to consider this association. Published studies in English of adults aged 18 or over were considered. At least 70% of study participants were required to be diagnosed with PTSD with a duration of 3 months or more, according to DSM or ICD criteria determined by clinician diagnosis or an established diagnostic interview. Co-morbidity was allowed as long as PTSD was the primary diagnosis; this led to the exclusion of studies that solely focused on populations with comorbid PTSD and SUD. There were no

restrictions based on symptom severity or trauma-type.

2.2. Search strategy

2.2.1. Search method for identification of studies

This systematic review and narrative synthesis were undertaken alongside a review of the efficacy of psychological therapies for PTSD for an update of The International Society for Traumatic Stress Studies treatment guidelines (International Society of Traumatic Stress Studies (ISTSS) [Online], 2018). A search was conducted by the Cochrane Collaboration, which updated a previously published Cochrane review with the same inclusion criteria (Bisson et al., 2013). This search produced a group of RCTs related to the psychological treatment of PTSD in adults. Data on factors associated with treatment outcome were extracted from these papers.

2.2.2. Data extraction and management

Study characteristics and outcome data were extracted by one reviewer using a pre-designed data extraction spreadsheet. The outcome measures for the review were both diagnostic status and magnitude of change over time, measured by the reduction in the severity of PTSD symptoms at the end of treatment using a standardized measure. When available, clinician-ratedd measures were included in the narrative review (e.g. Clinician Administered Post Traumatic Stress Scale (CAPS)) (Blake et al., 1995). If no clinician rated measure was used or reported, self-report measures were included (e.g. PTSD Checklist for DSM-5 (PCL-5)) (Weathers et al., 2013). Study authors were contacted to obtain missing data and if any clarification was required.

We specifically looked for and extracted information on the following variables that had previously been identified within the literature to be associated with treatment outcome in PTSD, anxiety and depression: (1) age; (2) gender; (3) ethnicity; (4) marital status; (5) employment status; (6) university education; (7) history of psychological intervention; (8) current use of psychotropic medication; (9) type of trauma; (10) time since trauma; (11) time of onset of symptoms after trauma; (12) duration of trauma; and (13) number of traumatic events. This list was not intended to be exhaustive and information on other factors considered was extracted if present.

2.2.3. Data synthesis

The a priori intention was to undertake a meta-analysis. However, there was limited data reported in the studies identified by this review and, when collected, the data were inconsistent in terms of measures used and time points. Therefore, it was decided to undertake a narrative synthesis as opposed to a meta-analysis, in order to synthesis the data in as meaningful a way as possible. Information on factors associated with treatment outcome was tabulated. Factors were coded as either (a) not reported (the factor was not reported in the paper); (b) no association (the factor was reported to have no bearing on treatment outcome); (c) significant increase (the factor was associated with a significant increase in PTSD symptom severity or diagnostic change); or (d) significant decrease (the factor was associated with a significant reduction in PTSD symptom severity or diagnostic change). Due to variation in follow-up time points, the factors were studied as close to the end of treatment as possible.

3. Results

3.1. Systematic search results

The update search for the ISTSS treatment guideline in March 2018 included 114 RCTs. Twelve additional RCTs were identified in an updated search and included in this review, which resulted in 126 eligible RCTs. Fifteen of these RCTs reported on factors associated with treatment outcome; 111 authors were contacted for additional information, 87 responded, 19 supplementary analyses of RCTs were received and reviewed for eligibility. Nine did not meet inclusion criteria as they did not report any factors associated with treatment outcome. This resulted in a total of 126 eligible studies and 25 (20%%) RCTs reported on factors associated with treatment outcome. Figure 1 presents a flow diagram for study selection, and Table 1 presents a summary of the factors associated with treatment outcome.

3.2. Characteristics of included studies

The number of randomised participants ranged from 10 to 837. Studies were conducted in Australia (9), Canada (2), China (2), Denmark (1), Germany (5), Iran (2), Israel (1), Italy (2), Japan (1), the Netherlands (8), Norway (1), Portugal (1), Romania (1), Rwanda (1), Spain (1), Sweden (3), Syria (1), Thailand (1), Turkey (3), Uganda (2), UK (11), and USA (77). Participants were traumatised by military combat (28 studies), sexual assault or rape (9 studies), war/persecution (9 studies), road traffic accidents (6 studies), earthquakes (4 studies), childhood sexual abuse (9 studies), political detainment (1 study), physical assault (2 studies), domestic violence/Intimate partner violence (4 studies), trauma from a medical diagnosis/emergency (3 studies) and crime/organised violence (4 studies), and interpersonal violence (1 study). The remainder (56 studies) included individuals traumatised by a variety of different traumatic events. There were 27 studies of females only and 9 of

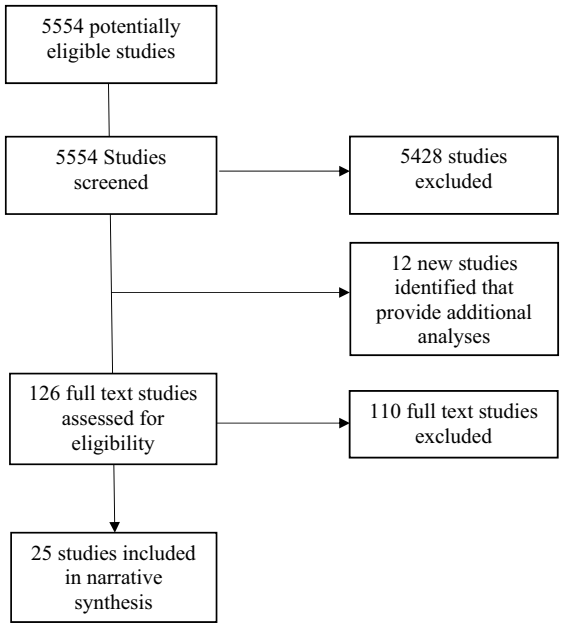

Figure 1. Study flow diagram.

Table 1. A summary of the factors affecting PTSD treatment outcome.

Factors associated with Treatment Outcome	Number of studies with a negative association with treatment outcome	Number of studies with a positive association with treatment outcome	Number of studies with no association with treatment outcome
Factors considered in two or more studies			
Adherence to homework		2	1
Age (younger)			3
Concurrent psychotropic medication			2
Diagnosis of anxiety			1
Diagnosis of depression	2		
Gender of participant			6
Higher education		1	5
Higher severity of PTSD at baseline	1		7
Less time since trauma		2	3
Low income			2
Lower severity of PTSD at baseline		1	
Married		1	3
Number of psychotherapy sessions/modules			3
Unemployment			2
Factors considered in one study only			
Ability to describe internal experiences		1	
Ethnicity (non-Hispanic white or other)			1
Greater dorsal lateral activation		1	
Greater startle response during virtual reality		1	
High emotional regulation (anger management and general emotion regulation capacity)		1	
History of psychiatric illness			1
Improvement in negative regulation		1	
Interpreter presence during therapy			1
Received higher no of psychotherapy treatment previously			1
Reduction in depression and anxiety over the course of therapy			1
Refugee status			1
Stressors outside of therapy (not specified)			1
Therapeutic alliance		1	
Therapist gender			1
Therapy type (Eye Movement Desensitisation and Reprocessing (EMDR) versus Imaginal Exposure and Cognitive Restructuring (E+ CR)			1
Type of trauma			1

only males; the percentage of females in the remaining studies ranged from 2% to 96%. Participant populations were mostly from the general public (89 studies), followed by military personal/veterans (37 studies), asylum seekers and refugees (8 studies), genocide survivors (1 study) and incarcerated women (1 study). Table 2 presents the characteristics of all the studies.

Table 2. Characteristics of all the studies reviewed.

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Population	% Unemployed	% University Educated
(Acarturk et al., 2016)	EMDR	WL			Refugees	Unknown	4
(Adenauer et al., 2011)	NET (CBT-T)	WL			Refugees	Unknown	Unknown
(Ahmadi, Hazrati, Ahmadizadeh, & Noohi, 2015)	EMDR	REM Desensitization	WL		Military Personnel/Veterans	Unknown	33.3
(Akbarian et al., 2015)	Group CBT-T	MC/RA			General Population	Unknown	Unknown
(Asukai, Saito, Tsuruta, Kishimoto, & Nishikawa, 2010)	PE (CBT-T)	TAU			General Population	Unknown	Unknown
(Basoglu et al., 2005)	Single-session CBT-T	WL			General Population	Unknown	5.1
(Basoglu et al., 2007)	Single-session CBT-T	MC/RA			General Population	Unknown	10
(Beck, Coffey, Foy, Keane, & Blanchard, 2009)	Group CBT-T	MC/RA			General Population	54	Unknown
(Bichescu, Neuner, Schauer, & Elbert, 2007)	NET (CBT-T)	Psychoeducation			General Population	0%	72
(Blanchard et al., 2003)	CBT-T	SC	WL		General Population	Unknown	Unknown
(Bradshaw, McDonald, Grace, Detwiler, & Austin, 2014)	OEI	WL			General Population	0	Unknown
(Brom, Kleber, & Defares, 1989)	CBT-T	Psychodynamic Therapy	WL		General Population	49	Unknown
(Bryant, Moulds, Guthrie, & Dang, 2003)	CBT-T	SC			General Population	Unknown	Unknown
(Bryant et al., 2011)	CBT-T	SC			General Population	84%	Unknown
(Buhmann, Nordentoft, Ekstroem, Carlsson, & Mortensen, 2016)	CBT-T	WL			Refugees	Unknown	Unknown
(Butollo, Karl, König, & Rosner, 2016)	CPT (CBT-T)	DET			General Population	Unknown	Unknown
(Capezzani et al., 2013)	EMDR	CBT-T			General Population	Unknown	Unknown
(Carletto et al., 2016)	EMDR	RT			General Population	Unknown	Unknown
(Carlson, Chemtob, Rusnak, Hedlund, & Muraoka, 1998)	EMDR	RT	TAU		Military Personnel/Veterans	62	Unknown
(Castillo et al., 2016)	Group PE/CT	WL			Military Personnel/Veterans	44%	Unknown
(Chard, 2005)	Group + Individual CPT	WL			General Population	Unknown	Unknown
(Cloitre et al., 2002)	CBT-T	WL			General Population	24%	52
(Cloitre et al., 2010)	STAIR (CBT-NTF)	CBT without a trauma focus			General Population	31%	Unknown
(Cloitre et al., 2016)	STAIR/EXP	STAIR/SupC	SupC/EXP		General Population		
Cooper & Clum, 1989)	Imaginal Flooding	Standard Group Treatment			Veterans		
(Cooper, Zoellner, Roy-Byrne, Mavissakalian, & Feeny, 2017)	PE	Sertraline			General Population		
(Devilly, Spence, & Rapee, 1998)	EMDR	TAU			Military Personnel/Veterans	Unknown	Unknown
(Devilly & Spence, 1999)	EMDR	CBT-T			General Population	Unknown	Unknown
(Dorrepaal et al., 2012)	Group Stabilising Treatment	TAU			General Population	83%	Unknown
(Duffy, Gillespie, & Clark, 2007)	CT (CBT-T)	WL			General Population	Unknown	Unknown
(Dunne, Kenardy, & Sterling, 2012)	CBT-T	WL			General Population	31%	73
(Echeburua, De Corral, Zubizarreta, & Sarasua, 1997)	CBT-T	RT			General Population	Unknown	20
(Ehlers, Clark, Hackman, McManus, & Fennell, 2005)	CT (CBT-T)	WL			General Population	25%	35
(Ehlers et al., 2003)	CT (CBT-T)	MC/RA			General Population	Unknown	Unknown
(Ehlers et al., 2014)	CT (CBT-T)	SC	WL		General Population	23	26
(Falsetti, Resnick, & Davis, 2008)	Group CBT-T	WL			General Population	Unknown	Unknown
(Fecteau & Nicki, 1999)	CBT-T	WL			General Population	Unknown	Unknown
(Feske, 2008)	PE (CBT-T)	TAU			General Population	29%	90%
(Foa, Rothbaum, Riggs, & Murdock, 1991)	PE (CBT-T)	CBT without a trauma focus	Supportive counselling	WL	General Population	Unknown	Unknown
(Foa et al., 1999)	PE (CBT-T)	CBT without a trauma focus	WL		General Population	38%	41%

(*Continued*)

Table 2. (Continued).

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Population	% Unemployed	% University Educated
(Foa et al., 2005)	PE (CBT-T)	WL			General Population	17%	34%
(Foa et al., 2018)	Spaced PE (CBT-T)	PCT	MC/RA		Military Personnel/Veterans	100%	66%
(Fonzo et al., 2017)	PE (CBT-T)	WL			General Population	Unknown	Unknown
(Forbes et al., 2012)	CPT (CBT-T)	TAU			Military Personnel/Veterans	36%	Unknown
(Ford, Steinberg, & Zhang, 2011)	CBT without a trauma focus	PCT	WL		General Population	Unknown	22%
(Ford, Chang, Levine, & Zhang, 2013)	TARGET (CBT-T) Trauma Affect Regulation: Guide for Education and Therapy	Group Supportive Counselling			Incarcerated Women	Unknown	Unknown
(Galovski, Blain, Mott, Elwood, & Houle, 2012)	TARGET-Group (CBT-T)	MC/RA			General Population	Unknown	Unknown
(Gamito et al., 2010)	VRE (CBT-T)	Control Exposure	WL		Military Personnel/Veterans	Unknown	Unknown
(Gersons, Lamberts, & Van der Kolk, 2000)	BEP (CBT-T)	WL			General Population	Unknown	Unknown
(Gray, Budden-Potts, & Bourke, 2019)	RTM (CBT-T)	WL			Military Personnel/Veterans	Unknown	Unknown
(Haagen et al., 2017)	EMDR + Stabilization	Stabilization			Refugees and Asylum Seekers		
(Hensel-Dittmann et al., 2011)	NET (CBT-T)	CBT without a trauma focus			Asylum Seekers	Unknown	Unknown
(Hien et al., 2017)	COPE + PE	Relapse Prevention Therapy	Active monitoring control group		General Population		
Hinton et al., 2005	CBT-T	WL			Refugees	Unknown	Unknown
(Hinton, Hofmann, Rivera, Otto, & Pollack, 2011)	Group CBT-T	WL			General Population	Unknown	Unknown
(Hogberg et al., 2007)	EMDR	WL			General Population	Unknown	Unknown
(Hollifield, Sinclair-Lian, Warner, & Hammerschlag, 2007)	Group trauma-focused CBT	WL			General Population	Unknown	40%
(Ironson, Freund, Strauss, & Williams, 2002)	EMDR	PE (CBT-T)			General Population	Unknown	Unknown
(Ivarsson et al., 2014)	I-CBT	WL			General Population	8%	65%
(Jacob, Neuner, Maedl, Schaal, & Elbert, 2014)	NET (CBT-T)	WL			Genocide Survivors	Unknown	Unknown
(Jensen, 1994)	EMDR	WL			Military Personnel/Veterans	68	Unknown
(Johnson, Zlotnick, & Perez, 2011	CBT without a trauma focus	TAU			General Population	73	7%
(Johnson, Johnson, Perez, Palmieri, & Zlotnick, 2016	CBT without a trauma focus	TAU			General Population	77	5%
(Karatzias et al., 2007)	EMDR	E+ CR			General Population		
(Karatzias et al., 2011)	EMDR	EFT			General Population	37	47%
(Keane, Fairbank, Caddell, & Zimering, 1989)	CBT-T	WL			Military Personnel/Veterans	Unknown	Unknown
(Krupnick et al., 2008)	Group IPT	WL			General Population	80	13%
Kearney et al., 2013	MBSR	TAU			Veterans		
(Krakow et al., 2000)	Imagery rehearsal	WL					
(Kubany, Hill, & Owens, 2003)	CBT-T	WL			General Population	Unknown	Unknown
(Kubany et al., 2004)	CBT-T	WL			General Population	Unknown	Unknown
(Laugharne et al., 2016)	EMDR	PE (CBT-T)			General Population	Unknown	Unknown
(Lee, Gavriel, Drummond, Richards, & Greenwald, 2002)	CBT-T	EMDR			General Population	Unknown	Unknown
(Lewis et al., 2017)	I-CBT	WL			General Population	19	62%
(Littleton, Grills, Kline, Schoemann, & Dodd, 2016)	I-CBT	I-Psychoeducation			General Population	Unknown	Unknown
(Litz, Engel, Bryant, & Papa, 2007)	I-CBT	I-SC			Military Personnel/Veterans	Unknown	Unknown
(Lindauer et al., 2005)	BEP	WL			Police officers		
Marcus, Marquis, & Sakai, 1997	EMDR	TAU			General Population	Unknown	Unknown
(Markowitz et al., 2015)	IPT	PE (CBT-T)	Relaxation Therapy		General Population	21	Unknown
(Marks et al., 1998)	PE (CBT-T)	Cognitive Restructuring	PE (CBT-T) (CBT-T)(CBT-T)and Cognitive Restructuring	Relaxation without PE (CBT-T) (CBT-T)(CBT-T)or CR	General Population	54	Unknown

(*Continued*)

Table 2. (Continued).

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Population	% Unemployed	% University Educated
(McDonagh et al., 2005)	PE (CBT-T)	PCT	WL		General Population	17	Unknown
(McLay et al., 2011)	VRE (CBT-T)	TAU			Military Personnel/Veterans	Unknown	Unknown
(McLay et al., 2017)	VRE (CBT-T)	CET			Military Personnel/Veterans	Unclear	Unclear
(Monson et al., 2012)	Couples CBT-T	CET			General Population	40	Unknown
Monson et al., 2006	CPT (CBT-T)	WL			Military Personnel/Veterans	Unknown	Unknown
(Miyahira et al., 2012)	VR	Minimal attention			Active military		
(Morath et al., 2014)	NET (CBT-T)	WL			Refugees	Unknown	Unknown
(Mueser et al., 2008)	CBT-T	WL			General Population	Unknown	Unknown
(Nacasch et al., 2011)	PE (CBT-T)	TAU			Military Personnel/Veterans	63	Unknown
(Neuner et al., 2010)	NET (CBT-T)	TAU			Refugees	Unknown	Unknown
(Neuner et al., 2008)	NET (CBT-T)	TAU	Monitoring		Refugees	49	Unknown
(Neuner, Schauer, Klaschik, Karunakara, & Elbert, 2004)	NET (CBT-T)	SC	Psychoeducation		Refugees	28	Unknown
(Nijdam, Gersons, Reitsma, de Jongh, & Olff, 2012)	BEP (CBT-T)	SC			General Population	Unknown	30
(Pacella et al., 2012)	PE (CBT-T) (CBT-T)	EMDR			General Population	Unknown	Unknown
(Paunovic, 2011)	CBT-T	MC/RA			General Population	74	11
(Peniston & Kulkosky, 1991)	CBT-T	WL			Military Personnel/Veterans	Unknown	Unknown
(Polusny et al., 2015)	MBST	PC-GT			Veterans		
(Pigeon, Allen, Possemato, Bergen-Cico, & Treatman, 2015)	PCBMT	Primary Care			Veterans		
(Power et al., 2002)	EMDR	TAU	WL		General Population	Unknown	Unknown
(SAM Rauch et al., 2015)	PE (CBT-T) (CBT-T)	CBT-T			Military Personnel/Veterans	Unknown	Unknown
(Ready, Gerardi, Backscheider, Mascaro, & Rothbaum, 2010)	VRE (CBT-T)	PCT			Military Personnel/Veterans	Unknown	Unknown
(Reger et al., 2016)	VRE (CBT-T)	PCT	WL		Military Personnel/Veterans	Active duty	7
(Resick et al., 2015)	CPT-Group	PE (CBT-T)			Military Personnel/Veterans	0	8
(Resick, Nishith, Weaver, Astin, & Feuer, 2002)	CPT (CBT-T) (CBT-T)	Group PCT	Minimal Attention		General Population	Unknown	Unknown
(Resick et al., 2017)	CPT (CBT-T) (CBT-T)	PE (CBT-T)			Military Personnel/Veterans	100	19
(Rothbaum, 1997)	EMDR	Group CBT-T			General Population	19	43
(Rothbaum, Astin, & Marsteller, 2005)	PE (CBT-T)	WL	WL		General Population	Unknown	Unknown
(Sautter, Glynn, Cretu, Senturk, & Vaught, 2015	Couples CBT without a trauma focus	EMDR			Military Personnel/Veterans		
Sautter et al., 2016	SAT	PTSD family education intervention			Veterans	12	75
Scheck, Schaeffer, & Gillette, 1998	EMDR	Couples Psychoeducation			General Population	Unknown	Unknown
Schnurr et al., 2003	Group CBT-T	SC			Military Personnel/Veterans	51	Unknown
(Schnurr et al., 2007	PE (CBT-T) (CBT-T)	Group PCT			Military Personnel/Veterans	38	Unknown
(Schnyder et al., 2011)	BEP (CBT-T)	Group PCT			General Population	Unknown	Unknown
(Schoorl, Putman, Van Der Werff, & Van Der Does, 2014)	ABM	AC			General Population		
(Shemesh et al., 2011)	IET	Control education condition			General Population		
(Sloan, Marx, Bovin, Feinstein, & Gallagher, 2012)	WET	MC/RA			General Population	78	41
(Sloan, Marx, Lee, & Resick, 2018)	WET	WL			General Population	Unknown	13
(Smyth, Hockemeyer, & Tulloch, 2008)	Expressive Writing; writing about their traumatic experience	Control Group (writing about time management)			Veterans		
(Spence et al., 2011)	I-CBT	CPT (CBT-T)				41	Not Clear

(*Continued*)

Table 2. (Continued).

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Population	% Unemployed	% University Educated
(Stenmark, Catani, Neuner, Elbert, & Holen, 2013)	NET (CBT-T)	WL			Refugees	Unknown	25
(Suris, Link-Malcolm, Chard, Ahn, & North, 2013)	CPT (CBT-T)	TAU			Military Personnel/Veterans	43	16
(Stirman et al., 2018)	Cognitive processing therapy with trauma account	Cognitive Processing Therapy without trauma account			General Population		
(Taylor et al., 2003	PE (CBT-T)	PCT	EMDR		General Population	13	Unknown
(Stapleton et al., 2006)	PE	EMDR	Relaxation Therapy		General Population	Unknown	Unknown
(ter Heide, Mooren, Kleijn, de Jongh, & Kleber, 2011)	EMDR	Stabilization			Asylum Seekers and Refugees		
(Tylee, Gray, Glatt, & Bourke, 2017)	RTM (CBT-T)	Relaxation Therapy			General Population		
(Vaughan et al., 1994	CBT-T	WL	EMDR		General Population	Unknown	Unknown
(Wells, Walton, Lovell, & Proctor, 2015)	PE (CBT-T)	RT	WL		General Population	6	Unknown
(Wells & Sembi, 2012)	CBT without a trauma focus	CBT without a trauma focus			General Population	Unknown	Unknown
(Wittmann et al., 2012)	BEP	Minimal attention Control Condition			General Population		
(Wilson et al., 1995)	EMDR	WL			General Population		
(Yehuda et al., 2014)	PE (CBT-T)	WL			Military Personnel/Veterans	Unknown	Unknown
(Zang, Hunt, & Cox, 2014)	NET (CBT-T)	MC/RA			General Population	Unknown	Unknown
(Zang, Hunt, & Cox, 2013)	NET (CBT-T)	WL			General Population	Unknown	Unknown
(Zlotnick et al., 1997)	Group CBT-T	WL			General Population	Unknown	33

Acronyms
ATM = Attentional bias modification
BEP = Brief Eclectic Psychotherapy
CBT = Cognitive Behavioural Therapy
CBT-T = Cognitive Behavioural Therapy with a Trauma focus
CET = Control Exposure Therapy
COPE = Concurrent treatment of PTSD
CPT = Cognitive Processing Therapy
CR = Cognitive Restructuring
CT = Cognitive Therapy
RTM = Reconsolidation of Traumatic Memories
DET = Dialogical Exposure Therapy
E + CR = Imaginal Exposure + Cognitive Restructuring
EFT = Emotional Freedom Technique
EMDR = Eye Movement Desensitisation and Reprocessing
I-CBT = Internet-based Cognitive Behavioural Therapy
IET = Imaginal Exposure Therapy
I-Psychoeducation = Internet-based Psychoeducation
IPT = Interpersonal Psychotherapy
I-SC = Internet-basedd Supportive Counselling
MBSR = Mindfulness-Based Stress Reduction
MC/RA = Medical Checks/Repeated Assessments
NET = Narrative Exposure Therapy
NTF = Non-Trauma Focussed
OEI = Observed and Experimental Integration
PCBMT = Primary Care Brief Mindfulness Training
PCGT = Present Centred Group Therapy

PCT = Present Centred Therapy
PE = Prolonged Exposure
REM Desensitization = Rapid Eye Movement Desensitization
RT = Relaxation Therapy
SAT = Structured Approach Therapy
SC = Supportive Counselling
STAIR + SupC = Skills Training in Affective and Interpersonal Regulation + Supportive Counselling
STAIR = Skills Training in Affective and Interpersonal Regulation
TAU = Treatment as Usual
TARGET (CBT-T) Trauma Affect Regulation: Guide for Education and Therapy
VR = Virtual Reality
VRE = Virtual Reality Exposure
WET = Written Emotion Therapy
WL = Waiting List

3.3. Factors associated with treatment outcome

3.2. Clinical characteristics

Symptom Severity: Severity of PTSD symptoms at baseline was one of the most commonly reported factors examined in relation to treatment outcome. The majority of studies that examined this association (n = 7 studies) found that PTSD symptom severity scores at baseline had no association with treatment outcome (Basoglu, Salcioglu, & Livanou, 2007; Ehlers et al., 2003; Haagen, Ter Heide, Mooren, Knipscheer, & Kleber, 2017; Karatzias et al., 2007; Lewis et al., 2017; Schnyder, Müller, Maercker, & Wittmann, 2011; Wittmann, Schnyder, & Buchi, 2012). However, findings were not consistent: one study reported that the most severe PTSD symptoms at baseline were associated with benefiting less from treatment (Cloitre, Petkova, Su, & Weiss, 2016).

3.2.1.1. Comorbid symptomatology. Comorbid diagnosis of depression was associated with significant increase in PTSD symptom severity in two studies (Haagen et al., 2017; Cloitre et al., 2016) which found those with a diagnosis of depression did less well in treatment compared to those without the diagnosis.

3.2.1.2. Aspects of treatment. Three studies found that the number of sessions or modules completed was not associated with treatment outcome (Haagen et al., 2017; Karatzias et al., 2007; Lewis et al., 2017). Concurrent use of psychotropic medication was not associated with treatment outcome (Ivarsson et al., 2014; Karatzias et al., 2007).

3.2.1.3. Time since trauma. One study found that more recent trauma was associated with a slightly improved effect (Lewis et al., 2017). However, three papers found that time since trauma had no association with treatment outcome (Basoglu et al., 2007; Ehlers et al., 2003; Karatzias et al., 2007).

3.2.1.4.. Type of trauma. One study found no association between the type of trauma and treatment outcome (Karatzias et al., 2007).

3.3. Patient characteristics

Younger Age was found to have no association with treatment outcome in three studies (Basoglu et al., 2007; Karatzias et al., 2007; Lewis et al., 2017).

Education was considered in six studies; one found that those who had completed higher education had greater treatment effect (Lewis et al., 2017); and five studies found no association between years of education and treatment outcome (Basoglu et al., 2007; Basoglu, Salcioglu, Livanou, Kalender, & Acar, 2005;

Ivarsson et al., 2014; Krakow et al., 2000; Wilson, Becker, & Tinker, 1995)

Employment status had no association with treatment outcome in two studies (Ivarsson et al., 2014; Karatzias et al., 2007).

Adherence to homework was found to be positively associated with treatment outcome in two studies (Marks, Lovell, Noshirvani, Livanou, & Thrasher, 1998) (Dorrepaal et al., 2012), but one study found no association with the amount of time spent on completing homework and treatment outcome (Spence et al., 2011). Completion of homework was associated with better outcomes for patients with fewer years of formal education compared to those who reported more years of education (Stirman et al., 2018).

Marital status was associated with greater gain from treatment in one study (Wilson et al., 1995) yet had no association with treatment outcome in three other studies (Ivarsson et al., 2014; Krakow et al., 2000; Karatzias et al., 2007).

Lower household income was reported to not have any association with treatment outcome in two studies (Krakow et al., 2000; Wilson et al., 1995).

Gender of participants was reported in seven studies to have no association with treatment outcome (Basoglu et al., 2007; Blanchard et al., 2003; Haagen et al., 2017; Ivarsson et al., 2014; Karatzias et al., 2007; Lewis et al., 2017; Wilson et al., 1995).

3.4. Other factors identified

Better emotional regulation was positively associated with treatment outcome in two studies, one found an association with better functioning (Cloitre et al., 2016) and one with greater reduction in PTSD (Hien, Lopez-Castro, Papini, Gorman, & Ruglass, 2017). Furthermore, low emotional dysregulation was associated with a reduction in substance abuse (Hien et al., 2017) and improvements in negative mood regulation (Cloitre, Koenen, Cohen, & Han, 2002). Three other studies found that the number of previous traumas had no association with treatment outcome (Basoglu et al., 2007, 2005; Haagen et al., 2017).

One study found that participants who were able to describe their internal experiences, thoughts, emotions and sensations in a non-judgemental manner were associated with a significant reduction in CAPS score (Possemato et al., 2016).

Ethnicity was not found to be associated with treatment outcome in one study (Krakow et al., 2000). Refugee status (Haagen et al., 2017) and the presence of stressors during the treatment (Stapleton, Taylor, & Asmundson, 2006) had no association with treatment outcome. Table 2 presents a summary of the factors associated with treatment outcome and Table 3 presents the characteristics of the papers that reported any factors associated with treatment outcome.

4. Discussion

This was the first systematic review to consider factors associated with treatment outcome of psychological treatments for PTSD. Whilst a number of factors have been found to be associated, the evidence is limited and inconsistent. A comorbid diagnosis of depression and higher levels of PTSD symptom severity at baseline were associated with poor treatment outcome (Hepgul et al., 2016). We also found some evidence that higher education, adherence to homework, and experience of more recent trauma were associated with better treatment outcome.

The association of comorbidity of depression with poor treatment outcome is recognised (National Institute for Health and Care Excellence [NICE], 2018) although the exact mechanism is unknown. One possible explanation (Angelakis & Nixon, 2015) considers emotional processing theory whereby successful treatment depends on the modification of traumatic memory structures that underlie emotions, via activation (engagement) of the fear structure through exposure and subsequent habituation (Jaycox, Foa, & Morral, 1998). Patients are required to emotionally engage during treatment and thus process traumatic memories. An inability to fully experience emotional affect (emotional numbing) in depressed patients may lead to under activation (under engagement) of the fear structure.

Alternatively, depressed patients may be more prone to use avoidance strategies such as overgeneralizing traumatic memories, which inhibit the full experience of negative emotions and successful habitation is prevented (Angelakis & Nixon, 2015). Rumination and overgeneralization may result in an over engagement for those who experience comorbid depression and risk them becoming overwhelmed by the emotional intensity of treatment and reduce its efficacy for PTSD (Rauch & Foa, 2006). It is important to recognize that psychiatric comorbidity might impact treatment planning and outcome.

PTSD symptom severity at baseline was associated with benefiting less from treatment but this was not a uniform finding and several studies found no association of baseline symptom severity and treatment outcome. It has been suggested that marked avoidance can interfere with the processing of the traumatic experiences due to the lack of engagement in therapy (Foa & Kozak, 1986; Resick & Schnicke, 1992) and the association of higher levels of avoidance of thoughts and feelings pre-treatment with higher rates of PTSD symptom severity post-treatment supports this (Gutner, Rizvi, Monson, &

Table 3. Characteristics of the studies: The following are studies that report any factors associated or not associated with treatment outcome of psychological therapies of PTSD.

Study	Country	Intervention	Participants	Type of trauma	Factors associated (or not) with treatment outcome
(Basoglu et al., 2005)	Turkey	Single-session CBT	59	Earthquake	Greater PTSD severity, higher education and past trauma had no significant association with treatment outcome as measured by the CAPS-IV but it was associated with less improvement in the Patients Global Impression (a self-measure that reflect a patient's belief about efficacy of treatment).
(Basoglu et al., 2007)	Turkey	Single-session CBT	31	Earthquake	Age, gender, education, past psychiatric illness, history of past trauma, time since the earthquake, and the pre-treatment clinical ratings were not significantly associated with treatment outcome.
(Blanchard et al., 2003)	USA	Trauma focused CBT	98	Road Traffic accidents	There was no main effect or interaction with therapist gender or no main effect of gender of patient to treatment outcome.
(Cloitre et al., 2002)	USA	CBT-T	58	Various	Predictors of improvement were therapeutic alliance and improvement in Negative mood regulation as measured by the NMR as measured by the CAPS. Significant reduction posttreatment in depression and anxiety were not associated with PTSD symptom severity reduction.
(Cloitre et al., 2016)	USA	Skills training in affective and interpersonal regulation (STAIR) followed by Prolonged Exposure (EXP)	104	Childhood sexual and physical trauma/ abuse	Higher emotional regulation predicted better functioning. Those with high 'Symptom burden' (PTSD, depression, dissociation and interpersonal problems) was associated with worse treatment outcome, and did least well in exposure, moderately well in skills and best in the combination as measured by the PTSD symptom severity, assessed via the CAPS.
(Dorrepaal et al., 2012)	Netherlands	Stabilizing Group Treatment	71	Child Abuse	Diagnosis of Borderline Personality Disorder (BPD) was associated with greater compliance, defined by completed treatment, as opposed to those without the personality diagnosis.
(Ehlers et al., 2003	UK	Cognitive Therapy (CT)	85	Road Traffic accident	Neither time since trauma nor the degree of change in PTSD severity (PDS) score with self-monitoring were associated with outcome.
(Fonzo et al., 2017)	USA	Prolonged Exposure (PE)	66	Not specified	Less Blood Oxygen Level Dependent activation (signal) in the brain at baseline was associated with greater reductions in symptom scores in the waiting list group in two right and two left dorsolateral prefrontal clusters. Finally, greater dorsal anterior cingulate activation at baseline was associated with greater reductions in symptom scores in the treatment group but not in the waiting list group
(Galovski et al., 2012)	USA	Modified Cognitive Processing Therapy (M-CPT)	100	Various	Treatment dropouts were younger, had fewer years of education and had lower annual household income and significantly higher pre-treatment CAPS severity at baseline assessment. Participant age, time since index trauma and pre-treatment CAPS and Beck Depression Inventory-II scores were identified as potential predictors of length of therapy.
(Haagen et al., 2017)	Netherlands	Eye Movement Desensitization and Reconsolidation and Stabilization (EMDR-S).	72	Various	Patients with severe levels of depression at baseline as measured by The Hopkins Symptom Checklist had progressively less PTSD symptom reduction over time. A diagnosis of major depressive disorder was predictive of poor treatment response, indicating that patients with a major depressive disorder improved less than patients without a major depressive disorder. None of the other predictors (pre-treatment PTSD severity, refugee status, interpreter presence during therapy, the number and nature of traumatic events, gender, number of psychotherapy sessions, and treatment dropout) were significantly associated with treatment outcome.

(*Continued*)

Table 3. (Continued).

Study	Country	Intervention	Participants	Type of trauma	Factors associated (or not) with treatment outcome
(Hien et al., 2017)	USA	Concurrent Treatment of PTSD and SUD using Prolonged Exposure (COPE).	110	Various	Baseline emotional dysregulation (ED) severity moderated treatment outcomes such that high ED was associated with greater reduction in PTSD severity among those who received COPE relative to RPT and AMCG. In contrast, low ED as association with greater reduction in substance use among those in RPT relative in COPE and AMCG.
(Ivarsson et al., 2014)	Sweden	Guided Internet Delivered Cognitive Behaviour Therapy for PTSD.	62	Various	Participant lost to follow-up were on average younger compared to those who completed the study. Gender, age, marital status, highest educational level, unemployment status, psychopharmacological medication and history of psychotherapy were not associated with treatment outcome.
(Karatzias et al., 2007)	UK	Eye Movement Desensitisation and Repro- cessing (EMDR) vs Imaginal Exposure and Cognitive Restructuring (E+ CR)	48	Various	Higher pre- to post-treatment CAPS total change score was significantly associated with fewer sessions and a lower baseline CAPS total score. Age, gender, marital status, occupation, type of trauma, time since trauma, therapy type, number of sessions, psychotropic medication, CAPS total (baseline), HADS-A, HADS-Dwere not associated with treatment outcome, as measured by pre and post CAPS severity scores.
(Krakow et al., 2000)	USA	Imagery Rehearsal Therapy (IRT)	169	Sexual assault	Demographic covariates; ethnicity, marital status, annual income, or education were not significant in any of the analyses.
(Kubany et al., 2004)	USA	Cognitive Trauma Therapy for Battered Women (CTT-BW)	125	Domestic Abuse	Comorbidity with depression, low self-esteem, younger age, less educated, and more shame prone at the initial assessment were associated with non-completers of treatment.
(Lewis et al., 2017)	UK	Internet-based guided self-help	42	Various	There was no significant effect modification by age, gender, baseline CAPS score, number of modules completed, or number of therapist minutes. However, more recent trauma experienced a slightly improved effect. Higher education was associated with greatest treatment effect, and those with a higher degree experiencing greater improvement in CAPS scores.
(Marks et al., 1998)	UK	Prolonged Exposure (PE) Vs Cognitive restructuring	87	Various	Adherence to homework was associated with more improvement on the Global Improvement scale.
(McDonagh et al., 2005; Possemato et al., 2016)	USA	Primary Care Brief Mindfulness Training (PCBMT) Cognitive Behavioural Therapy (CBT)	6274	Military Trauma Child Sexual Abuse	The ability to describe internal experiences, thoughts emotions and sensations, in non-judgemental way was associated with decrease in PTSD symptoms. Participants who dropped out of CBT endorsed more depression and greater anxiety, reported lower quality of life, and endorsed more distorted schemas on The Traumatic Stress Institute Beliefs Scale (TSI; Pearlman, 2001) than those who stayed in treatment.
(Possemato et al., 2016; Schnurr et al., 2003)	USA	Trauma-focused Group Psychotherapy Primary Care Brief Mindfulness Training (PCBMT)	36,062	Military Trauma	Individuals who were lost to follow-up had lower Global Assessment of Functioning scores, were more likely to be unemployed and have a lifetime history of substance abuse or dependence. The ability to describe internal experiences, thoughts emotions and sensations, in non-judgemental way was associated with decrease in PTSD symptoms.
(Schnurr et al., 2007; Schnurr et al., 2003)	USA	Prolonged Exposure (PE) vs Present-centred therapy (PCT). Trauma-focused Group Psychotherapy	277,360	Female Veterans Military Trauma	Participants in Present Centred Therapy received an increase or new medication during the study compared to those in the prolonged exposure group. Exploratory analyses to determine whether medication change during treatment modified the treatment effect for CAPS severity scores indicated that the interaction between medication change and treatment was not significant. Individuals who were lost to follow-up had lower Global Assessment of Functioning scores, were more likely to be unemployed and have a lifetime history of substance abuse or dependence.

(*Continued*)

Table 3. (Continued).

Study	Country	Intervention	Participants	Type of trauma	Factors associated (or not) with treatment outcome
(Schnurr et al., 2007; Spence et al., 2011)	USA	Internet delivered Cognitive Behavioural Therapy (I-CBT) for PTSD. Prolonged Exposure (PE) vs Present-centred therapy (PCT).	125,277	Various Female Veterans	There was no significant relationship between post-treatment outcome the amount of time spent on the homework or with the amount of time spent on thought challenging. Participants in Present Centred Therapy received an increase or new medication during the study compared to those in the prolonged exposure group. Exploratory analyses to determine whether medication change during treatment modified the treatment effect for CAPS severity scores indicated that the interaction between medication change and treatment was not significant.
(Spence et al., 2011; Stirman et al., 2018)	USA	Cognitive Processing Therapy (CPT). Internet delivered Cognitive Behavioural Therapy (I-CBT) for PTSD.	140,125	Sexual or physical violence Various	Completing homework was associated with a greater decrease in PTSD symptom severity score, as measured by the PTSD symptom scale (PSS). There was no significant relationship between post-treatment outcome the amount of time spent on the homework or with the amount of time spent on thought challenging.
(Stapleton et al., 2006; Stirman et al., 2018)	USA	Prolonged Exposure (PE)Cognitive Processing Therapy (CPT).	60,140	Various Sexual or physical violence	No evidence that treatment outcome varied as a function of the pre-treatment severity of anger or guilt. Additional presence of stressors had no associated with treatment outcome. Completing homework was associated with a greater decrease in PTSD symptom severity score, as measured by the PTSD symptom scale (PSS).
(Stapleton et al., 2006; Wilson et al., 1995)	USA	Eye Movement Desensitization and Reprocessing (EMDR) Prolonged Exposure (PE)	8060	Various	PTSD-I scale symptom severity at baseline, years of education, income, gender, gender of therapist were not associated with treatment outcome. Participants who were married were associated with greater gain. No evidence that treatment outcome varied as a function of the pre-treatment severity of anger or guilt. Additional presence of stressors had no associated with treatment outcome.
(Wilson et al., 1995)	USA	Eye Movement Desensitization and Reprocessing (EMDR)	80	Various	PTSD-I scale symptom severity at baseline, years of education, income, gender, gender of therapist were not associated with treatment outcome. Participants who were married were associated with greater gain.

Resick, 2006; Krause, Kaltman, Goodman, & Dutton, 2008; Pineles et al., 2011). This suggests a possible need for interventions specifically focused on improving treatment engagement.

Higher education was associated with better treatment outcome. This could be due to the impact of educational background on understanding of psychological interventions and ability to fully engage in them. For example, trauma-focused CBT requires written homework, and more advanced literacy skills may facilitate better outcomes (Fairburn, 1995). Moreover, research has suggested that low educational status is a barrier to adherence to psychological intervention for PTSD because of greater difficulties in understanding the interventions' content, which may result in a lack of motivation to engage in treatment (Waller & Gilbody, 2009).

Homework adherence was associated with better treatment outcome. People with PTSD vary greatly in their ability to complete homework assignments, due to various factors, including a mismatch between ability and difficulty of the homework assignment, or motivation/commitment on the part of the person with PTSD or the therapist. Strategies for improving participation in homework may increase the potential of completing homework assignments to enhance treatment outcome (NICE, 2018).

More recent trauma was associated with better treatment outcome. One explanation for these findings is that the secondary psychosocial consequences that trauma survivors may experience contribute to the emergence or continuation of other negative events (e.g. unemployment, partner separation and financial difficulties), which can increase PTSD or maintain already existing disorders (Freedy, Kilpatrick, & Resnick, 1993). These events themselves can lead to psychological distress, disruption of social relationships, and other psychosocial difficulties. For example, studies have observed an increase in alcohol

and drug use after the experience of a traumatic event (Grieger, Fullerton, & Ursano, 2003), which can increase the likelihood of relapse and clinical worsening of symptoms. Some investigators contend that the post-trauma period can be characterized by an adverse social environment, defined as "a consistent pattern of chronic (negative) impacts to individuals and communities" (Picou, Marshall, & Gill, 2004). A meta-analysis has examined comparative outcomes and acceptability of different PTSD treatments (Merz, Schwarzer, & Gerger, 2019). However, the research was limited to 12 RCTs and, unlike our review, only included studies that directly compared one type of treatment with another. No treatment approach was found to be superior at the end of treatment, although psychotherapeutic treatment shown greater benefit than pharmacological treatment at last follow-up. The lack of long-term findings further limits the research and demonstrates the need for large-scaled comparative trials providing long-term follow-up data.

5. Strengths and limitations

Our work has a number of strengths including its adherence to rigorous systematic review methodological standards and the synthesis of data obtained from RCTs. However, limiting our review to RCTs may have excluded studies with other research designs that may also have reported on associations with treatment outcome. A meta-analysis was not considered appropriate due to the heterogeneity between studies and lack of consistent reporting. An alternative approach is meta-analysis of individual participant data (IPD), in which raw individual level data are obtained and used for synthesis (Simmonds et al., 2005). However, the resources and time required for such analysis is considerable and may limit their use. There are also some issues with the included studies that limit interpretation; for example, they adopted strict inclusion criteria which often excluded patients with active substance dependence, acute suicidal ideation, and major depressive disorder, all of which have been associated with greater severity of PTSD (Back, Brady, Jaanimagi, & Jackson, 2006; Clark, Masson, Delucchi, Hall, & Sees, 2001; Najavits et al., 2003). This may have resulted in the exclusion of participants from more vulnerable and, potentially, treatment-resistant populations, which limits the generalisability of the findings. That said, although the use of more pragmatic inclusion criteria (e.g. patients with substance misuse) may enhance generalizability, it may be difficult to then determine the true effects of the intervention and to whom the results apply. Finally, only the first author extracted and synthesised data from studies. However, data extraction followed the standardised criteria for narrative synthesis (Popay et al., 2006), thereby ensuring a standardised process across studies. Furthermore, frequent meetings with the review team were to discuss progress and interpretation of the results.

Overall, it is difficult to draw firm conclusions from this review due to the limited strength and consistency of evidence for the association of specific factors with treatment outcome. For example, a depression diagnosis and homework adherence were only found to be predictive in two studies, although the evidence was consistent. This contrasts with PTSD symptoms severity where only one of eight studies found an association with poorer outcome, the others finding this was not associated with outcome. Further research is required to determine the true nature of associations found in this review. As the systematic search is over 18 months old, an updated review may also provide additional information.

6. Clinical implications

The review has highlighted a current lack of knowledge in relation to factors associated with the treatment outcome of PTSD. This is further complicated by the inconsistency of reported factors and the variance in treatment outcome among patients with PTSD. It is unreasonable to expect that a simple explanation for variance in treatment outcome will be found for a mental health condition with such clinical and pathophysiological diversity as PTSD (Weathers & Keane, 2007). The results of this review do not suggest that anyone should be excluded from receipt of treatment due to the presence of the factors considered. The association between various factors and treatment outcome that should, however, be taken into account when recommending and delivering specific treatments to people with PTSD. This highlights the need to move to a more personalized treatment approach (Medicine, 2011). Considering the current inconsistency, it is essential to consider other factors that may facilitate personalization of treatments, for example, neuroimaging and cognitive testing in addition to routinely collected clinical characteristics may provide 'a person with PTSD signature' that predicts response or non-response to different treatments.

On the basis that co-morbid depression was found to be associated with poor treatment outcome, clinicians should pay particular attention to adapting treatments to individuals' specific needs, including whether the initial targeting and treatment of PTSD symptoms will subsequently reduce

depression symptoms, or whether initial targeting of depressive symptoms is necessary before commencing PTSD treatment. This could determine the best approach for the greatest improvement of both disorders. The findings that higher education was associated with better treatment outcome suggest that particular care should be taken to make treatments fully accessible to people with PTSD with different levels of education. However, this is likely confounded by socioeconomic deprivation and requires further research to better understand the association. It may be that where treatment is ineffective alternative strategies are required such as the provision of additional support or adoption of models that minimize cognitive demand, while maximizing active processing of new information. For example, the use of an adapted form of Eye Movement Desensitisation Reconsolidation (EMDR) to suit the individual's level of cognitive and emotional functioning has been recommended (Tinker, 1999). This involved a short explanation of the treatment, visual cues instead of abstract language to represent feelings and physical gestures to help communication.

7. Research implications

A clear research implication from our work is the need for further work into the association of factors with PTSD treatment outcome and the reasons for these associations. The importance of exploring and reporting factors associated with treatment outcome cannot be overstated. Future treatment research should: (a) routinely examine and report factors that may be associated with or moderate outcome(s) to allow a better understanding of processes associated with treatment efficacy; (b) assess and report beyond the standard demographic and clinical variable(s) that are thought to influence outcome and consider a translational approach of combining neuroimaging, cognitive and genetic data to form a more detailed clinical phenotype. The direction of associations should also be considered with a view to identifying predictors of treatment outcome. This would provide empirical evidence that could inform the improvement of treatment efficacy, aid the development of new and better treatments and pave the way for a personalized medicine approach to the treatment of PTSD.

Complex PTSD (CPTSD), it is not known whether current established treatment provides the optimal outcome considering the usually prolonged and repeated nature of the trauma in CPTSD, as well as additional symptoms of disturbance of self-organisation. Whilst this review found a study that considered elements of disturbance of self-organisation (DSO) in the context of comorbid Borderline Personality Disorder (BPD), research is required to examine DSO in the context of individuals with a diagnosis of CPTSD to gain a better understanding of the effects of the additional symptoms on treatment outcome.

In order to improve the quality of data on factors associated with treatment outcome, a more universal reporting style must be adopted. The CONsolidated Standards of Reporting Trials (CONSORT) (Bennett, 2005) guidelines were specifically developed to eliminate inadequate reporting of RCTs. However, the guidelines do not address other facets of reporting that may require attention, namely factors associated with treatment outcome. As the CONSORT checklist provides guidelines to improve the completeness of the study, we suggest that the following additional factors are considered for inclusion: (a) characteristics of the participants (age, gender and ethnicity); (b) clinical characteristics (severity, chronicity, comorbidity, and prior treatment exposure), (c) social and economic variables (income, employability, living arrangements); (d) self-efficacy and social support (relationships, family and friends). These factors should be documented at baseline, during and after treatment in order to understand their association to treatment outcome at every stage. In cases of Complex PTSD, consideration of disturbances of self-organization and treatment outcome may also be important for treatment selection (Briere, Kaltman, & Green, 2008; Cloitre et al., 2009). This information will further our understanding of how these observed factors are associated with successful or unsuccessful outcome, and help clinicians and researchers design or adapt evidence-basedd interventions to reduce ineffectiveness.

There is also a need to develop more multidimensional-standardisedd measures of treatment outcome. Traditionally, and importantly, trials have focused on reduction of PTSD symptoms and rates of remission. In addition, measures of the acceptability of the treatment are also required, such as: (a) adherence (consisting of attendance to therapy and homework completion); (b) retention rates (the reasons people continued on with treatment, or withdrew); and (c) attitudes to treatment (to identify patient experiences and perspectives through semi-structured interviews). These additional measures will facilitate consistent reporting and a greater understanding of factors likely to be associated with treatment outcome.

A key research challenge is to develop an evidence base that facilitates a comprehensive understanding of the factors associated with treatment outcome. It is likely that these factors will vary across populations and people but some commonality is to be expected. The factors

identified in this systematic review and narrative synthesis provide a useful starting point to meet this challenge and will, hopefully, stimulate the generation of a more rigorous and clinically relevant framework that can inform treatment selection in the future.

It is imperative that future studies explore factors associated with outcome. At this point, it is premature for firm conclusions to be made about the effect of the factors identified on treatment outcome. However, this study represents an important first step in discovering which treatments work best for whom and highlights the need for more research in this area to inform better treatment decisions, the development of better treatments and ultimately to achieve better outcomes.

Acknowledgments

We would like to thank Popay et al. for providing us with their unpublished guidance on narrative synthesis and to the many authors of included studies who responded to our requests for additional information.

Disclosure statement

No potential conflict of interest was reported by the authors.

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